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Construction of a Transcriptome Atlas of the Mouse Brain at Cellular Resolution

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DNA is the blueprint for the development and maintenance of organisms. In recent years, genome sequencing has revealed the detailed blueprint for many species, including human and its close genetic cousin, the mouse. Within such organisms, cells differentiate to assume specific functional roles; cells express different sets of genes, the sections of the blueprint activated to produce materials the cell uses to function.

In situ hybridization (ISH) is a powerful technique for revealing gene expression in individual cells, the level of detail necessary for investigating how genes control cell type identity, cell differentiation, and cell-cell signaling. Although the availability of high-throughput (HT) equipment for ISH enables the expeditious determination of expression patterns for thousands of genes in serially sectioned tissues, a large collection of ISH images is, per se, of limited benefit. But, via accurate detection of expression strength and spatial normalization of expression location across different specimens, ISH images become a minable digital atlas of gene expression capable of advancing functional genomics in a mode similar to DNA sequence databases.

This work has developed and deployed computational methods that automate HT-ISH image characterization. The automated procedure determines cellular expression strengths using signal detection, maps these into an anatomical atlas constructed using subdivision mesh models, and annotates the expression pattern distributions. The process has been applied to over 100 genes in the postnatal day 7 mouse brain. Results are stored in a publicly available database at www.geneatlas.org. At this online resource, traditional annotation-based searches for genes are available, as well as advanced customizable comparisons between genes in user-defined anatomical regions.

Supported by NSF grant ITR-0205671, and the Burroughs Wellcome Fund NLMT15LM07093 and NIHP41RR02250.